NON-TECHNICAL ABSTRACT

Molecular chemotherapy, the focus of this proposal, is a strategy based upon the delivery and selective expression of a gene encoded toxin into cancer cells to achieve- tumor eradication. Both conventional and molecular chemo-therapies rely on delivery of a toxin in order to eradicate tumor cells.
Conventional pharmacologic chemotherapy, however, is limited by a high level of nonspecific toxicity to normal cells. The concept of gene therapy improves upon conventional methodologies by allowing for selective delivery or selective expression of the toxin in order to improve the therapeutic effect. One toxin frequently utilized to accomplish molecular chemotherapy is the Herpes Simplex Virus Thymidine Kinase (HSV-TK) gene which is given in combination with intravenous Ganciclovir(GCV). Several investigators have developed clinical trials employing this methodology but have used recombinant retrovirus mediated gene transfer and relied solely upon bystander effect to achieve an anti-tumor effect. We intend to use an adenovirus vector to deliver the HSV-TK gene since this type of vector can be produced in high titer, can directly transfect target tissue regardless of whether cells are dividing, and has an established record of safety. The concept of molecular chemotherapy with direct transfection of target cancer cells represents a novel strategy that we intend to exploit in this protocol. We plan to study this novel therapy in patients with recurrent ovarian and extraovarian cancer. These cancers are deadly diseases and there are currently no curative treatments available. A single dose of this novel agent will be administered within the abdominal cavity of patients who participate in the study and GCV will be administered intravenously twice a day on days 3-I7. The major objectives of the study are to determine how much of the HSV-TK gene can be safely administered in combination with intravenous GCV and what are the expected side effects. In addition, we will determine if this novel compound actually transfects tumor cells. Although not a major endpoint to this study, we will also determine if this therapy will cause tumor regression.